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VB

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/776,044	02/26/97	BYWATER M	1614-178F

HM22/1013

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EXAMINER	
EYLER, Y	
ART UNIT	**PAPER NUMBER**
1642	16

DATE MAILED: 10/13/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/776,044	Applicant(s) Bywater et al.
	Examiner Yvonne Eyler	Group Art Unit 1642

☒ Responsive to communication(s) filed on *Jul 19, 1999* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-11 and 13-15* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-11 and 13-15* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. The request filed on 7/19/99 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/776044 is acceptable and a CPA has been established. An action on the CPA follows

Claims 1-11 and 13-15 are pending and under consideration in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

2. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119 (a-e) as follows:

The instant claims are drawn to sequencing of the complete coding region of p53 which was not disclosed or contemplated in the priority documents.

Claim Rejections Withdrawn:

3. The rejection of Claims 2-4, 10, 11, and 13 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of the amendments to the claims.

4. The rejection of Claims 2 and 3 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn.

5. The rejection of Claims 1-11 and 13 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn.

6. The rejections of Claims 1-12 and 13 under 35 U.S.C. 103(a) are rendered moot in light of the new grounds of rejection.

Claim Rejections Maintained and New Grounds of Rejection:

7. Claims 1-11, 13, 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims now recite limitations which were not clearly disclosed in the specification, as filed, and now change the scope of the disclosure. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

The specification, as filed, did not disclose or contemplate methods of diagnosis/prognosis comprising sequencing the complete coding region of p53. Applicant urges that support may be found in the experimental section where the complete nucleotide sequence was sequenced. The location where disclosure of the sequencing of the complete coding region of p53 cannot,

however, be found. The examples disclose the sequencing of 4 fragments of the coding region which encompass exons 2-11, but not the entire coding region (page 13).

8. Claims 1-10 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elledge et al. (Breast Cancer Res. Treat. 27:95-102, 1993) and of Callahan (J. Natl.Cancer Institute. 84:826-827, 1992) in view of Diamandis et al. (U.S.# 5,552,283)

The claims are drawn to a method of diagnosis/prognosis, and treatment guidance for cancer comprising sequencing the complete coding region of p53 to determine the presence and location of any mutations coupled with the determination of node status.

Elledge et al. teach that detection of p53 mutations at the nucleic acid level in neoplastic samples of node negative breast cancer is prognostic of micrometastasis and future recurrence. Elledge et al. further teach that the location of the mutations also served as a further indicator of prognosis, with mutations occurring in certain areas such as exon 7 being more indicative of an aggressive tumor phenotype (page 100). Finally, Elledge et al. teach that treatment decisions for intermediate sized tumors could well depend on such prognostic factors (page 97).

Callahan teaches that lymph node status is the primary, art standard, parameter in prognosis of breast cancer and in guiding decisions with regard to adjunct therapy. Callahan teaches, however, that a percentage of node (-) patients relapse and that additional prognostic factors in these situations would be desirable. Callahan teaches, in this light, that p53 mutation is an independent prognostic marker and suggests the combination of nodal status and p53 status to distinguish patients who require aggressive postsurgical therapy. See the entire article.

Thus the prognosis of cancer by determination of p53 mutations and location of mutations, combined with node status and the use of such prognostic determinations to direct treatment decisions was known in the art at the time the invention was made as taught by Elledge et al. and Callahan et al.

Elledge et al. and Callahan et al. differ from the instant invention in that they do not detect p53 mutations by sequencing the entire coding region of the gene.

Diamandis et al. teach that many diagnostic/prognostic methods to determine p53 mutations were known in the art from as early as 1992, including sequencing of the entire coding region but that sequencing of the entire coding region was the most accurate and specific of the methods. See the abstract; Figure 1; column 2, lines 13-27; column 5, lines 20-23.

It would have been *prima facie* obvious to one of ordinary skill in the art to modify the combination prognostic determinations of Elledge et al. and Callahan to include sequence determination of the entire coding region of p53 in order to ensure the accurate and specific detection of p53 mutations as taught by Diamandis et al.

Therefore, it would have been *prima facie* obvious to and one of ordinary skill in the art would have been motivated to automate the assay of Elledge et al. as modified by Callahan., with a reasonable expectation of success as taught by Lindstrom and Hedrum et al. in order to streamline and analyze multiple samples for prognostic information.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

10. Claim 11 is rejected under 35 U.S.C. 102(b) as being anticipated by Hollstein et al. (Science 253:49-53, 1991).

Hollstein et al. teach the determination of a mutation in the p53 gene by sequencing the coding region. See the entire article.

11. Claims 11 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Hedrum et al. (BioTechniques 17:118-129, 1994).

Hedrum et al. teach the detection of a mutation in p53 by sequencing of the entire genomic region encoding p53 (page 118, column 3) and further the sequencing by using solid phase techniques (see page 123, column 2).

12. Claims 11, 13 and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Diamandis et al. (U.S.# 5,552,283).

Diamandis et al. teach the determination of mutations in p53 by sequencing of the entire coding region and the use of such determination as a diagnostic/prognostic test. (See the abstract; Figure 1; column 2, lines 13-27; column 5, lines 20-23).

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yvonne Eyler, Ph.D. whose telephone number is (703) 308-6564. The examiner can normally be reached on Monday through Friday from 830am to 630pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached on (703) 308-2731. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**paula.hutzell@uspto.gov**].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Yvonne Eyler, Ph.D.
Patent Examiner
October 10, 1999